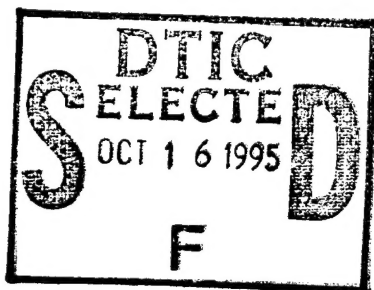


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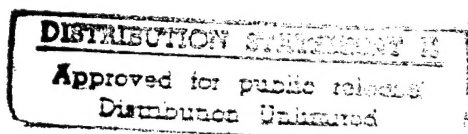


The Keystone Center
Scientist to Scientist Colloquium
1994 Proceedings

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THE KEYSTONE CENTER

Keystone Science and Public Policy Program • Keystone Science School
Keystone Symposia on Molecular and Cellular Biology

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**1994 SCIENTIST TO SCIENTIST COLLOQUIUM
PROCEEDINGS REPORT
TO
OFFICE OF NAVAL RESEARCH**

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THE KEYSTONE CENTER'S **1994 SCIENTIST TO SCIENTIST COLLOQUIUM** consisted of eight plenary sessions over five days, August 14 to August 19, 1994. The meetings took place in Keystone, Colorado, organized and facilitated under the direction of The Keystone Center. This report provides: (1) a brief description of the meeting; (2) a brief summary of how the \$25,000 grant was applied toward Colloquium expenses; (3) a summary of each scientific session including discussion comments if relevant; (4) a general description of the radio program produced from the meetings; and (5) a summary of participant evaluations.

USE OF FUNDS

The Office of Naval Research (ONR) grant of \$25,000 represented approximately 11% of the total 1994 budget for the Scientist to Scientist Colloquium. While grant monies have been applied to general expenses The Keystone Center incurs holding the meeting, including participant travel, lodging, and meal expenses, no monies were used toward costs incurred by attending government employees (of the 85 attendees, 9 were government employees). Please see the attached ONR FEDERAL CASH TRANSACTIONS REPORT (2 PAGES) AND KEYSTONE CENTER WORKSHEET.

INTRODUCTION

This is an interdisciplinary meeting of researchers at the forefront of science and technology in the United States and Europe. The 1994 Colloquium was the fourth Scientist to Scientist Colloquium. It has been said by many participants that it is the best meeting of its kind, and even the best scientific meeting they have attended. In 1994, 85 scientists, academicians, business and foundation executives, members of government and media participated in the five days of plenary sessions, small group informal gatherings, and outdoor activities. Twelve of the scientists were "junior" scientists (scientists under the age of 45) already making an impact in their fields. Eighteen participants were women. Five participants were people of color. Every effort is being made to increase the diversity of participants.

Each of the sixteen speakers was introduced by a scientist who provided background on the overall subject and area of particular research. Three of the introducers were Nobel Laureates. All speakers were highly accomplished, cutting-edge researchers.

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Scientist to Scientist Colloquium
August 14 - 19, 1994
PROGRAM AND SPEAKERS

<u>TOPIC</u>	<u>SUBTOPICS</u>	<u>SPEAKERS</u>
TERRESTRIAL DYNAMICS Topic Chair: Raymond Jeanloz	<i>K/T Extinctions</i>	Walter Alvarez - UC Berkeley
	<i>Tectonics</i>	Marcia McNutt - MIT
CANCER Topic Chair: Richard Peto	<i>Cancer & Tobacco</i>	Richard Peto - Oxford University
	<i>Tumor Suppressor Genes</i>	Curtis Harris - NIH
NEW MATERIALS Topic Chair: Philip Anderson	<i>Buckminsterfullerene</i>	Arthur Hebard - AT&T Bell Labs
	<i>High T_c Superconductivity</i>	Robert Birgeneau - MIT
SOLAR SYSTEM Topic Chair: Katherine Freese	<i>Jupiter Impact & Earth crossing Asteroids</i>	Eugene Shoemaker - USGS
	<i>New Objects in Solar System</i>	Jane Luu - Stanford University
MATHEMATICS Topic Chair: Jerome Friedman	<i>Molecular Dynamics</i>	Tamar Schlick - New York U.
	<i>Experimental Chaos</i>	Albert Libchaber - Princeton U.
MOLECULAR BIOLOGY OF SENSATION Topic Chair: Maxine Singer	<i>How Hearing Happens</i>	A. J. Hudspeth - SW Medical Ctr.
	<i>Making Sense of the Olfactory World</i>	Cori Bargmann - UC San Francisco
SYSTEMS NEUROBIOLOGY Topic Chair: David Baltimore	<i>Seeing Motion: From Neural Circuits to Perceptual Decisions</i>	William Newsome - Stanford U.
	<i>Brain Development</i>	Carla Shatz - UC Berkeley
BIRTH & AGE OF THE UNIVERSE Topic Chair: David Schramm	<i>Birth</i>	Andrei Linde - Stanford University
	<i>Age</i>	Robert Kirshner - Harvard University

SESSION SUMMARIES

Session I: Terrestrial Dynamics

The two session speakers were introduced by Dr. RAYMOND JEANLOZ, Professor of Geology & Geophysics at the University of California, Berkeley. Dr. Jeanloz pointed out that Dr. Marcia McNutt's work is at the cutting-edge of geology in the area of plate tectonics in that it is a study which is looking at the long term climatic evolution of the planet earth, a new area of research.

Dr. MARCIA MCNUTT, Professor of Earth & Atmospheric Sciences at the Massachusetts Institute of Technology, discussed her work with a team of scientists from the U.S. and China measuring uplift at the Tibet Plateau and the formation of Tibet itself. Their ability to access data kept by Chinese scientists which was previously inaccessible to the west is significant. Tibet is the largest topographic feature on earth and has the largest elevations on earth including, of course, the Himalayan chain. Geologists have held to several truths relating to why the Tibetan Plateau is the way it is, and one is that the crust beneath it is approximately twice the thickness of continental crust elsewhere on the planet. The crust is also lighter than the mantle beneath it, which makes it somewhat like an iceberg floating on the ocean. India used to be a separate sub-continent and it has been moving northward colliding (since 40 or 50 million years ago) with the southern margin of China -- confirmed with the finding of a suture zone where the two pieces meet-- the effects of the collision are very significant geologically in distant places, from the formation of the Sian mountains to the formation of Lake Baikal in Russia. Further, the impacts on global climate change are significant. Indian monsoons are created, causing flooding in Bangladesh and other areas while still other areas such as Gobi, Tarim, and the Tibet plateau itself are deserts. The troubling question for geologists is why evidence in core samples taken beneath the deep sea (in the Bay of Bengal and Arabian Sea) indicate monsoons began only 7 or 8 million years ago, a mystery given that the formation of the plateau took place so much earlier. Geologists and paleoclimatologists are trying to see if there is a connection between the steady decrease in the temperature of the earth (over a period of about 40 million years) and the increase in the rates of continental erosion (over the same period and due, they believe, to the uplift of Tibet). One theory proposed is that calcium carbonate given off in erosion combines with carbon dioxide in the atmosphere and then is dropped into the oceans and sequestered in deep sea beds.

During the discussion period a question was asked about how it is now known that Tibet is widening rather than rising, and the answer Dr. McNutt gave was that it is based on computer modeling where after a certain height the plateau can no longer support the weight, which would lead to widening out of the material making up the plate.

In regard to earth processes impacts are of major importance and are coming to be recognized, finally, as crucial to our planet's history, from climate to extinction and evolution of species. Dr. WALTER ALVAREZ, Head, Department of Geology & Geophysics at the University of California, Berkeley, discussed his work locating craters on earth created by the impact of asteroids, particularly at the boundary between the Cretaceous and Tertiary (K/T) periods. Walter Alvarez and his father, Luis Alvarez, have made the dinosaur extinctions a science whereas it has in the past been a great intellectual teaser, food for fantasies. The first question Dr. Alvarez posed in his talk was: have the changes in history been slow, gradual ones, or have sudden, quick changes been important, or even predominant? The history of the earth was for a long time based on uniformitarianism (from Sir Charles Lyell), and catastrophe was "bad." The historical records of *foraminifera*, single celled shelled animals became nearly extinct 65 million years ago, at the end of the Cretaceous period. The limestone from that period is full of these animals' shells, a limited number of them are found in the early Tertiary layer, and some went on to survive and evolve. With enough data collection it was also found that the iridium anomaly is always present at the boundary. An impact event has certain characteristics: a cylinder of hard vacuum where air has been pushed out of the way in front of the entering object, and air in front heats up to 20 Kelvin and, among other things, there is an ejecta curtain (solid and liquid debris being sprayed outward) found world wide. Winds and Tsunamis lead to cold and dark, followed by a greenhouse effect. Forest fires would have been started everywhere except where there is cloud cover. Acid rain (nitric acid and sulfuric acid) is a characteristic as well as an almost doubled carbon dioxide content. In 1991 geologists finally found evidence of an impact -- A crater at Chicxulub in Mexico, straddling the north coast of the Yucatán, which is thought to be the best candidate to explain mass extinctions at the K/T boundary. The area of the crater was first studied because the bed being researched looked like an impact tsunami deposit (they are rare): they have characteristically coarse sediment and tektites (little droplets of impact melted glass), shocked calcium carbonate which had bubbled up (at this particular spot there was a very carbon dioxide rich limestone platform), due to the fact that the continental margin is torn up and then slides up as a turbulent mixture of rippled sand (sand is not found normally in the sediment) and plants. Dr. Alvarez showed slides of the area of the Yucatan, and drawings of what would be actual impacts. There have been numbers of these events, based on numbers of large craters being discovered, one also very large event at 35 million years ago. He conjectures that if dinosaurs had not been wiped out at 65 million years ago (if the asteroid had hit at a slightly later time in our orbit) our human species would not be in the dominant position it is in today.

During discussion a question was raised about the theory of uniformitarianism and its impact on/relationship to Darwin's theory of evolution. It was argued that the (proven by evidence as described above, but still not accepted by the whole community) physical impacts on species is disproof of uniformitarianism but not of evolution. It was also pointed out that the evidence being discussed in this talk was not in support of the new theory of punctuated equilibrium.

Session II: Cancer

The two speakers, Dr. CURTIS HARRIS and Dr. RICHARD PETO, were introduced by (Nobelist) Dr. PAUL BERG, Cahill Professor in Cancer Research, Director of the Department of Biochemistry at Stanford University Medical Center. Dr. Berg's opening remarks provided a brief historical overview of the medical community's unfolding knowledge of cancer. He described cancer cells in addition to how cancer is now thought to be a genetic disease, either inherited directly or as a predisposition, and how cancer is age related. Further, by showing the life cycle of a cancer cell, Dr. Berg provided some key background biology which helped prepare the participants for the following two talks.

Dr. Curtis Harris, Chief, the Laboratory of Human Carcinogenesis at the National Cancer Institute, began by giving a recent history of cancer research that stemmed from work being done on RNA and DNA based viruses, work being done on round worms, on frog eggs, and on rodents. Dr. Harris explained that his own paradigm is humans -- why some are cancer prone and some not, looking at clinical observations in terms of what are the genetic mutations that occur in the tumor that might be important. Working with cultured human tissues and cells, Dr. Harris and his colleagues found that metabolism of a chemical carcinogen has almost as much variation as there are numbers of individuals. Those findings lead to further study regarding how and why people differ in susceptibility to carcinogens. In regard to the molecular genetics of cancer, what is important are the accumulated genetic changes, not necessarily a pattern or sequence of changes that have to occur. What are the cell's protective mechanisms against cancer? Dr. Harris discussed tumor suppressor genes, specifically P53, a protein transcription factor which has been found to be involved in controlling gene expression, in DNA replication, in programmed cell death, and is also thought to be involved in DNA repair. Importantly, it has been found that if a tumor is found to have a normal P53 gene, it is going to be much more responsive to traditional cancer therapy (which is based on the programmed cell death mechanism). This hypothesis is gaining quite a bit of evidence and, said Dr. Harris, hopefully researchers will begin to develop new therapies based on it.

Following Dr. Harris' talk, questions were asked about how certain carcinogens (cigarette smoke, for example) can damage the P53 gene. Dr. Harris explained that chemicals that enter the body are metabolized and may be activated through (primarily) oxidation, then they bind to the bases in DNA, disrupting the normal cell signalling processes, and lead to mutations; when the cell divides it replicates the mutations, driving tumor formation. Someone else wondered if normal P53 couldn't be put into cancer cells as a therapy to stop cancer from spreading. It was an interesting point since this is something scientists are looking into, but until the gene itself is better understood (knowing its 3-dimensional structure is just one problem) it is currently just a hope that it may someday be an answer.

Dr. Richard Peto, Epidemiologist with Oxford University Cancer Center, presented statistics on a variety of cancer deaths world wide, compared with death and birth rates. Dr. Peto focused particular attention on cancers from tobacco, as he feels tobacco is one of the most urgent health issues, needing more careful consideration by global health experts and officials. It was known in 1950, before Drs. Watson and Crick discovered DNA, that tobacco caused about 90% of lung cancer deaths in the United States. However, it is not known which of the many chemicals in cigarette smoke cause which kinds of cancers. By looking at the numbers Dr. Peto hopes to bring more attention to the seriousness of the link between tobacco and cancers. In the U.S. there are half a million cancer deaths per year, about 150,000 of those are lung cancer deaths, a large fraction of those are caused by tobacco (about 1/3rd of all U.S. cancer deaths are associated with tobacco). It is, however, difficult to link tobacco directly to many causes of cancer because of other influences, such as alcohol; studies indicate smokers drink more alcohol than nonsmokers; people with high cholesterol are at higher risk of dying from smoking. Tobacco use tends to increase the opportunities for other diseases to develop and become fatal. World wide there are about 3 million tobacco related deaths per year; two million with good incomes and one million poor. By the time children of today reach middle age (in the 2020s) the numbers will be 10 million deaths related to tobacco per year. Until about five years ago there were not sufficient statistics available to provide a realistic view of the importance of tobacco on mortality rates. Statisticians had been looking at the past rather than at the future. But it is the young people who smoke and continue to smoke (on average a pack of cigarettes per day) throughout their lives who are the largest statistic; the affects of smoking take some years to express themselves physiologically. Dr. Peto thinks that while breast cancers and prostate cancers are increasing, as well, they are not of the significance that reports would have us believe. One reason is because data show rates of incidence, and not just mortality. Looking at mortality rates, tobacco-causes are much more significant.

During discussion someone made the point that carcinogens in cigarette smoke are known to be mutagenic, and Dr. Peto responded that it is not known whether that is the key to what is fatal in cigarette smoke. Another question was raised about rates of premature death and population and whether or not more resources should really be put toward population control (because of its effects on the environment and global health) and Dr. Peto responded that yes, population control is an important issue, but preventing premature death might be a very important issue for those living now.

Session III: New Materials

DR. PHILIP ANDERSON, Nobelist, Professor of Physics at Princeton University, introduced the New Materials session providing a background on superconductivity, which was discovered in 1911 but remained unexplained until 1957 when the famous BCS theory provided a phenomenology of superconductivity as well as a mechanism. The characteristics of superconductive materials are a lot of free electrons per (metal) atom (Niobium is about the best example, having five free electrons), and magnetism in the materials is problematic. The transition temperature limit using the BCS mechanism is (or was) about 30 Kelvin. The new classes of superconductors, however, "violate these rules spectacularly." Arthur Hebard and Robert Birgeneau will be talking about two of these new classes of superconductors, the buckminsterfullerenes and the cooperates, respectively.

DR. ARTHUR HEBARD, AT&T Bell Labs: The focus of his talk was on carbon 60, the most symmetrical of all the buckminsterfullerenes, or buckyballs, in fact an almost completely spherical, soccerball-like structure has 60 equivalent carbon atoms and is, therefore, highly stable. C_{60} is referred to as the third form of carbon, the other two being graphite and diamond. C_{60} is an especially interesting and useful material because it is an "arrestingly beautiful molecular building block of a very unique intermediate size." It has a high electron affinity, it takes in atoms sort of like a sponge (it is half the density of diamond and is empty on the inside), which accounts for its effectiveness as a superconductor. Dr. Hebard discussed how the alkali metal doped fullerenes superconduct in an unexpected way. The ultimate state for conductivity is a half-filled electron band in the C_{60} molecule. Adding potassium, which likes to give up its electrons, provides one electron to the three in the outer C_{60} band, filling the band half way and making the molecule at optimal conductivity, as an ionic solid (versus a van der Waal solid); vibration (the molecules tumble) is also a key part of its conductivity. There are experiments being done now trying to make 2-dimensional compounds using C_{60} , since some of the highest T_c superconductors are 2-D, or quasi-2-D. Potential new commercial and scientific uses for C_{60} include photolithography, dielectrics, lubrication, tagging of hydrocarbon fuels, UV protecting cosmetics, optics, and CVD diamonds among others. The key to future applications of this material, said Dr. Hebard, is the intermediate length scale.

It was noted by geologists and astrogeologists during discussion that C_{60} is found in nature in pre-Cambrian rock, but how frustrating for scientists making the material that it dissolves in the presence of oxygen and hydrogen. On the other hand, since it has become so easy to produce the molecule in mass quantities in the laboratory, the fact that it does not occur widely in nature does not impede the science.

Dr. ROBERT J. BIRGENEAU, Dean of Science at the Massachusetts Institute of Technology presented a history, including his own work, in the field of high temperature superconductivity. As Dr. Phil Anderson explained, Dr.

Birgeneau's expertise is in the study of magnetism by neutron defraction, on of the most important experimental probes that has been used in high temperature superconductors. He has had success with his colleagues working with copper oxide ceramics which, he said, is a "physics of an extraordinarily different character from the conventional materials." The basis of this is that understanding the physics of a copper oxide sheet is not so simple. The numbers of layers of copper oxide influences the temperature, although more than three layers of copper and thallium (in between the sheets of copper) may lead to instability, but if thallium is replaced by mercury the temperature, under pressure, gets to 150 degrees Kelvin. It turns out that the stuff in between the copper is ultimately the source of the charge carriers that produce the superconductivity. Further, whatever is put in between the sheets of copper must be off stoichiometry, but the copper oxide sheets must be perfect. If the stuff inbetween is stoichiometric, the material will be an insulator, not a superconductor. Researchers are trying to solve problems in the physics of a 2-D system. Also important to understanding the new materials they are developing is in the spin of the electrons and the holes in between the atoms. What they are trying to understand is the fact that you can go from a non-magnetic insulator to the world's record in superconductivity by just adding a few holes to some copper oxide sheets. There is no theory to get from the insulator to the superconductor.

An anthropologist/biologist raised a question about fundamental problems in particle physics and a frontier of awareness where not being able to explain superconductivity because of problems (as Dr. Birgeneau indicated in his talk) with what is fundamental. A physicist doing research close to this question responded by pointing out that because of this issue there is a revolution in quantum mechanics having to do with magnetism and a complete turn around in the understanding about magnetism and superconductivity causing chaos because of the re-thinking involved around the issue. "It's almost as dramatic as re-thinking why the dinosaurs died."

Session IV: Solar System

Dr. JANE LUU and Dr. EUGENE SHOEMAKER were introduced by Dr. KATHERINE FREESE, professor of Astrophysics at the University of Michigan.

Dr. Jane Luu is Associate Professor of Astronomy at Harvard University (her present position; at the time of the conference she was Hubble Fellow at Stanford University). Dr. Luu, with her colleague Dr. David Jewitt (University of Hawaii), decided in 1987 to embark on a new survey of the outer solar system, the first survey using a CCD, or charged couple device. The CCD is a sensitive electronic detector in the form of a chip with 1,000 to 2,000 pixels on a side for taking very high resolution images through a telescope; the image is produced as an electrical signal that can be fed directly into a computer, allowing for faster than ever before astronomical computations. The telescope they used was the University of Hawaii's 2.2 meter, and with that set up they were able to detect objects as faint as the 25th magnitude, or

about 50 million times fainter than the limit of the human eye. They were seeking to answer a question raised by Gerard Kuiper in 1951: why would planetary accretion end at Pluto? It is now known that the space beyond Pluto contains a large population of "icy planetessimals" which are believed to be remnants from the formation of the planetary system, and it has been given the name The Kuiper Belt. Dr. Luu concentrated her talk on this "gravitationally unstable disc" and the evidence so far collected in the effort to prove its existence. A year after they began the survey a paper was published by three theorists: Duncan, Quinn and Tremaine; they presented the most convincing argument thus far for the existence of objects beyond Neptune. They were addressing the problem of short period comets, those comets with small orbits going out only to the distance of Jupiter with orbital periods of less than 200 years. On the other hand, the long period comets come from the Oort cloud located about 50,000 AU from the sun [Dr. Shoemaker describes it as "a cotton candy halo around the sun"], have large orbits with periods greater than 200 years. The precise orbits of some 150 comets that came from the Oort cloud are known. Evidence (some gathered by simulation) indicates that if a ring of trans-Neptunian bodies were formed during the early solar system, it would survive until today. If the Kuiper Belt is proven not to exist then astronomers would have no idea where the short period comets come from. In August of 1992 Luu and Jewitt detected an object with magnitude 23rd, their first Kuiper Belt object, called QB₁. In March of 1994 they discovered object EB₃, magnitude 23.3. A total of 13 trans-Neptunian objects have been found, nine by Luu and Jewitt, four by others. They range from 32 AU to 46 AU, and if these objects are at the inner edge of the Kuiper Belt, the Belt then starts somewhere beyond Neptune and extends out past Pluto. An object at 40 AU would have an orbital period of about 250 years. The Luu and Jewitt team made very rough limits of the mass and size of the Belt population, calculated from their discoveries so far: If the Belt is symmetrical about the plane of the ecliptic then the thickness of the Belt is about 16°; the projected area of the belt as seen from the earth is the thickness of 16° x 360° = 6,000° square. With a surface density of about 4 to 5 objects per square degree, the Belt must have a population of at least 30,000 objects with a diameter larger than 100 km. This implies a minimum Belt mass of about 10²³ kg or about .02 earth masses. These objects formed at such large distances from the sun would most likely consist of ice which aggregates from the pre-planetary disc; in other words Kuiper Belt objects represent the most primitive solar system material available for study, and probably are the building blocks of the giant planets and are likely to be precursors to short period comets. Another question Dr. Luu raised was the relationship of Pluto and its satellite Chiron to the Kuiper Belt, because basically they are proving to be in the middle of it. Not only that, but Pluto is 70% rock, is on a highly inclined and eccentric orbit, and somehow "captured" Chiron even though Pluto is only twice the size of Chiron. Information about the origins of these bodies might be found through discovery of the Kuiper Belt. What has not been worked out is how the objects get past Neptune.

Dr. Shoemaker talked about his work studying impact craters around the world, particularly in Australia and in the United States. His motivation for

doing this work was that he felt if he became the world's expert on the geology of craters on earth he might be able to go to the moon and study the craters there. He did become the world's expert on craters on the earth and moon, in spite of never having (yet) traveled to the moon. Dr. Shoemaker had observed that Australia provides an excellent study ground for impact craters because it is the stablest piece of continent on the planet, and he showed photographs of nine or ten craters in Australia, describing the features of ejecta: *breccia* including glass, shatter cones, as well as the tell-tale iridium and platinum anomalies. After nearly twenty years of studying rock and geological formation on earth, to discover what was hitting us Dr. Shoemaker looked to space. In 1973 he and his colleagues began a systematic study of what is "out there" using the highest quality telescopes and cameras in the world. That year, 13 earth crossing objects were identified, of that only four of the orbits were determined, enabling scientists to find them again. Today about 200 earth crossing asteroids are known, many of them are catalogued, about half of them have been located with the Schmidt telescope Dr. Shoemaker uses. There are fewer earth crossing asteroids than there are comets. The largest earth crossing asteroid is about 9 kilometers in diameter and there is only one of those. Larger bodies, or comets (70% rocky constituents, like carbonaceous meteorites, with a "tail" -- see the notes for Jane Luu's talk, above), cross the earth's orbit "frequently." It was on the 25th of March in 1993 that the Shoemakers, with David Levy, discovered the Shoemaker-Levy 9 comet. It soon attracted international attention, but some of the best images came from the telescope at Mauna Kea in Hawaii, and the work of Jane Luu, with her colleague David Jewitt. The orbit of the comet (which had been broken into about two dozen pieces) was determined in about four months, and it was calculated that the comet would hit Jupiter on July 25, 1994 (it actually hit between the 16 and 22 of July). All over the world predictions were being made and modelling was being done before this first-time-ever event. Dr. Shoemaker and Dr. Paul Hassig (Titan Corporation) modelled a 1 km diameter ball of ice, travelling 60 km per second, breaking apart at 31 km below the Jovian cloud top, the plume rises up about 800 km over 4 minutes and then starts to collapse and spread laterally; they ran the model to about 7 minutes and the plume about flattened out by that time. About five other groups tried similar calculations. The actual data came in (taken with the Hubble and Keck telescopes and others) with the plume from Nucleus A (the first piece of the comet to hit Jupiter) rising from the clouds at about 3 minutes, and the plume falls and flattens in about the same amount of time as the Shoemaker-Hassig model suggested. The differences in the real data and their model were due to the make up of the comet (it was more complicated than a piece of ice), but in terms of total energy released Dr. Shoemaker feels they were not far off. What they did not predict, but felt they probably should have, was that a hydrogenated soot would result from the largest impacts, leaving a black spot. Dr. Carl Sagan's lab has been simulating this in their studies about the origin of life. Is there periodicity to the collisions? The question was asked, and Dr. Shoemaker replied that it's pseudo-periodicity, that for the last 210 million years (where the evidence is more available than it is for before that time) there was a certain stepped frequency of events connected to mass extinctions, at (B.P.) 35 million years, 65 million years, 92 million years, and 210 million years.

Session V: Mathematics

JEROME FRIEDMAN (Nobel) Professor of Physics at Massachusetts Institute of Technology introduced Albert Libchaber of the NEC Research Institute and Princeton University, and Tamar Schlick of New York University. The first talk addressed the subject of experimental chaos. Dr. Friedman gave a brief introduction saying that chaos is a method to study the time evolution of complicated systems, which are generally non-linear. One of the important features of chaos is a great sensitivity to initial conditions, which are not possible to get in the real world. In chaotic systems there is always a time scale in which the behavior of that system becomes stochastic, it cannot be predicted and in general divergence can be very great. This is the introduction to Dr. Albert Libchaber's talk.

To demonstrate his work, Dr. Libchaber described an experiment with gas (SF_6) and heat which interact at the beginning in an orderly, simple pattern later exhibiting complex behavior. The attempt is to produce a crystal of air, using a cell (box) constructed of a cold top plate (made of transparent sapphire), a hot bottom plate adding a flux of heat from below. As the heat increases, convection sets in, and eventually at very high heat turbulence develops. The heat is increased by the Rayleigh number until a bifurcation line is reached where the system becomes time dependent. What at first is a well-defined frequency becomes more and more complex. This is one step in the development of complexity. With a decrease in cell size, a change to a low viscosity gas such as helium, and an increase in Rayleigh number, turbulence is achieved. A histogram can be done of the hot and cold showing exponential distribution. A hypothesis is that the state of turbulence has some similarity with high energy physics -- turbulence leading to a bifurcation to new states with new excitations. Dr. Libchaber proposed that in order to have two more regimes that he could imagine the SSC would have been useful, because it would have been necessary to use a lot of helium and to get beyond a Rayleigh number of 10^{16} one would need helium gas 3 meters high at low temperature, and to get beyond that would need 10 meters high of helium.

Participants asked which features of the results were understood theoretically and which were not and the reply was that the onset of convection is understood, one of the modes of rolling waves is understood, oscillatory instability is understood, and when it comes to turbulence, only the 27 scaling of turbulence is understood. Also, plumes can be understood with scaling, but plumes in turbulent fluid are not understood. Unfortunately, scientists studying nonlinear systems do not have tools designed specifically for studying strongly nonlinear systems.

"Whatever complexity means, most people agree that biological systems have it." (Franfelder and Wolness).

DR. TAMAR SCHLICK, Associate Professor in the Chemistry and Mathematics Departments at New York University addressed the work she has been involved in, called "Molecular Dynamics." As Dr. Friedman said in the introduction to her talk, it is important to the understanding of the collective motions of proteins; biological activity is dependent on collective motion, so it is important to understand time scale in order to understand biological systems. This field is at the crossroads of mathematics, biology, chemistry, physics, and computer science, and there are many possible applications to medicine. Molecular Dynamics (MD) is needed to explain the wide range of thermally accessible states of the system and we need it to explore the fundamental structure-function relationship in biology. From MD simulation (on computers) it is possible to obtain information on atomic fluctuation, on conformational transition, enzyme substrate binding and, ultimately, perhaps, protein folding. The equations of motion derived from the simulations are fundamental because they relate to three key quantities: time, configuration and energy. It has been shown through MD simulations that the lock and key model is untrue, because it isn't possible to hold one group rigid to bring in the other, rather that mobility of both is crucial to functioning. It was pointed out by a biologist in the audience that knowing the characteristics in this way it is possible to develop inhibitors to bind to the active site and repress certain unwanted biological activities. Numerically in order to solve the equations from MD simulations one integrates Newton's equations of motion numerically because the systems are too complex, the forces are nonlinear so cannot be solved analytically. With standard integration methods it's necessary to resolve the high frequency for numerical stability, a property of the difference equation, and when there is instability the coordinates and velocities grow uncontrollably in magnitude and the results are meaningless. Another aspect of Dr. Schlick's work is called DNA supercoiling and trefoil knotting. Studying the biochemistry, enzymology, differential geometry, topology and dynamical aspects of this supercoiling, the interactions of DNA with other macromolecules, and the interconversions among topological isomers also leads to a greater understanding of biological function.

Session VI: The Molecular Biology of Sensation

DR. MAXINE SINGER, President, The Carnegie Institute of Washington, introduced the session. Dr. Singer illustrated how all multi-cellular organisms begin from one cell, a fertilized egg cell. She explained cells' processes of becoming differentiated, taking on specific characteristics and functions; how specificity comes after the "turning on" and "turning off" of genes, and this is in part influenced by the spatial relationship of cells to other cells around them. Cells' ability and need to talk with each other has particular importance, and this communication is highly specific ("unlike at your home when someone's knocking, you at first don't know who's there, but the cell knows exactly who's knocking and what the message is"). Cells

periphery of the body receive environmental stimuli and pass it along to the brain. This sensory perception is a complex process being more clearly understood through research conducted by such scientists as Jim Hudspeth and Cori Bargmann.

Dr. A. J. HUDSPETH is Director of the Neuroscience Program at the University of Texas Southwestern Medical Center, and is a Howard Hughes Medical Institute Investigator. Beginning with the nerve cell, one of the very specialized cells Dr. Singer was referring to in her introduction, it can be understood how "information" gets around the body, allowing the body to respond and perform its functions, such as, particularly important in regard to Dr. Hudspeth's work, hearing. Another key cell involved in the hearing process is called a hair cell, it is the sensory cell of the internal ear, giving us the capacity to hear airborne sound. Given our ability to hear sounds at frequencies as great as 20 kilohertz, and to detect movement at about the dimension of a sodium ion, those hair cells are technically advanced. Also, given that 9% of the U.S. population is hard of hearing or deaf, Dr. Hudspeth and others want to know what are the types and causes of damage to these hair cells. The cells are vectorial, responding in chemically different ways to being moved in different directions. We measure gravity with these cells, so it turns out that it is important that they be able to report the direction of the stimulus as well as its absolute magnitude. By applying a thin (a micron in diameter) glass probe to the hair cell that measures its stiffness and electrodes to record the response of the hair cell when moving, they discovered a nonlinearity in the system. That is, the ear distorts sound, and that distortion is due to "adaptation." The sensitivity to sound changes places in the ear, depending on the position of the hair bundle and length of time it's in that position. Further, inbetween hair bundles is a spring, called a tip link, that can be broken if the bundle is pushed too far.

Dr. CORI BARGMANN, Assistant Professor in the Departments of Developmental Biology & Genetics, and the Department of Anatomy, University of California at San Francisco is conducting research on the olfactory system. Her work involves research on the nervous system of a soil worm, *Caenorhabditis elegans* (*C. elegans*), from knowledge of the anatomy of the human nervous system, and from behavioral studies in a variety of vertebrate and invertebrate species. The questions she and her colleagues are looking to answer are: How are scent molecules (going by in the air) recognized? How does the olfactory system discriminate between various molecules? How do we assign qualities (meanings) to molecules (smells)? Dr. Bargmann pointed out that some of the meanings can be innate, as in the example of mother and child recognizing each other by pheromones. Olfactory queues are under control of the olfactory system as well as an organ, the vomeronasal organ, which is a specialized part of the nose (not known to exist in humans until recently). It is now known that olfactory neurons express more than one receptor, and may express several. There are 10 million neurons in the vertebrate olfactory system, but humans are known to have the ability to discriminate only 10,000 odorants. By studying a simple system, such as that in *C. elegans*, neurobiologists are trying to understand what the nose tells the brain. An interesting finding in these studies with *C. elegans* is that when all but one of

the neurons are destroyed the worm loses its ability to discriminate between very similar molecules, but maintains the ability to discriminate between very different molecules. Using classical genetics the biologists ask what kinds of molecules do single neurons use to discriminate between different molecules in the environment? And, which genes are required to detect different molecules? By first mutagenizing neurons in some of many worms and then by using behavioral screens, a process that takes about two years (a similar example in human studies is the case of searching for the gene for Huntington's Disease, which took about 50 people working for about 10 years). What has become known is that neuronal activity feeds back on neuronal development and that the environment affects neuronal development. Carla Shatz discusses this phenomenon in her talk on brain development.

Questions following the talk brought up a parallel between the olfactory system and the immune system regarding the recognition of many different molecules. The sizes of the molecules entering the system may have something to do with the ability to recognize, and it may be more specific in the olfactory system. Another interesting characteristic of the olfactory system is the regeneration of neurons, which is different from other neurons in the body. That brought up the question of memory and where the memory is stored, in the neurons or in the brain, or how it is stored in both. This is an area of new research.

Sesson VII: Systems Neurobiology

Dr. DAVID BALTIMORE, Nobelist (for his work in immunology) and Professor of Biology at Massachusetts Institute of Technology, introduced the two talks of this session talking about the difficulties neurobiologists face in understanding the nervous system and its integration. The first problem is that, although most cells of the body have largely interchangeable parts (liver cells, for example, interact with each other), nerve cells are not interconnected as other groups of similar cells are. Nerve cells are specialized to perform very particular functions. And most nerve cells are post-mitotic, they do not divide and replicate (the exception, as pointed out by Dr. Cori Bargmann, are olfactory neurons). It is important that once the wiring is set up that it's fixed; this is particularly relevant in learning and memory. Carla Shatz will discuss how wiring is set up in the brain, and Bill Newsome will discuss how resynthesis occurs in the process of perceiving motion.

DR. CARLA SHATZ, Class of 1943 Professor of Neurobiology, the University of California at Berkeley: Dr. Shatz focused her talk on how neuronal connections are made between the eyes and the brain. How this wiring is set up is parallel to the way wiring is set between the other organs and the brain. This wiring mostly takes place in the fetus, and environmental stimuli completes the process very early in life after birth. These are massively parallel systems. It is understood by neurobiologists that during development there are markers, like road signs, that lead the neuronal axons to their

targets -- say, from the eye to the visual target in the brain. It has been recently learned that it is a layering process that occurs the same way around every time, but it isn't yet understood why. There may be half a million nerve cells in the eye that need to connect to half a million nerve cells in the target area of the brain (the Lateral Geniculate Nucleus, or LGN). There are then velcro-like molecules, called cell adhesion molecules, that allow for appropriate recognition (chemo-attraction) and hold the two neurons together when they meet; inappropriate connections are avoided (with chemo-repulsants). Precision of connectivity in the nervous system probably determines behavioral capacity. In the eye, for example, the neuronal connections have to be precise for visual acuity -- incomplete connections could make a grainy image, like a Seurat painting. At a certain stage in development, the molecular markers that are involved in setting up the wiring have done their job and disappear. Future re-wiring is therefore not possible. There are about 10^{11} neurons in the brain, plus or minus one or two orders of magnitude; each neuron may make hundreds or thousands of connections. But there are only 10^5 genes in the whole genome, so there are clearly not enough genes to wire up the nervous system to the degree of precision that is known to exist. The trick to wiring lies in neural activity itself: feedback from firings between neurons determines whether or not the "glue" sticks. So, genetically, all that is needed is a code for the feedback mechanism. Timing is also a factor, called a correlation-based mechanism, and a spatial requirement that neighboring neurons need to be correlated in their firing. Recent work with electrodes implanted in an animal fetus' retina and then attached to a computer and the histogram shows that there is a regular firing pattern in waves. The final hypothesis Dr. Shatz has made based on these observations is that cells that fire together in the developing retina wire together in the target (LGN).

A question was asked about how the "highways" are set up, allowing the road markers (chemical messengers to the neurons) to be on the right coordinates. Dr. Shatz said that in the early embryo the cells have positional identity. Another scientist raised the question of how rods and cones develop in humans versus how it develops in other animals who may need to see clearly earlier than we do. Dr. Shatz pointed out that in every vertebrate the rods are developed last, but lower vertebrates use their eyes from the moment they hatch, and they have a mechanism to allow it, whereas we are still developing vision when we are born.

Dr. WILLIAM NEWSOME, Professor of Neurobiology at the Stanford University School of Medicine discussed "Neural Foundations of Visual Motion Perception." The central question driving his research is: how do physiological events in the brain relate to visual perception and visually guided behavior? He studies motion detection in awake, behaving macaque monkeys. Fine wire electrodes are placed in their visual cortexes and the behavioral situation is changed to test discrimination ability. On the neuronal level activity can also be modified to see if there can be predictable impacts on the judgements made about what is being seen. It is this latter experiment that was the focus of his talk. After describing the cerebral

cortex Dr. Newsome focused the attention on the striate cortex (V1) at the back of the brain. It turns out that over half of the surface area of the cerebral hemisphere is devoted to processing visual information, revealing the paramount importance of vision in primate behavior. The electrodes are inserted into the visual cortex and action potentials are recorded. Scientists doing this research are trying to see if there is a pattern of visual stimulation that would excite cells at the back of the cortex. By mapping the area they have discovered over 30 visual areas in the macaque. It turns out that there is some division of labor among the areas, for instance the area of the temporal lobe is involved in object recognition, a dorsal area that terminates in the parietal lobe seems to be involved in spatial judgements.

Session VIII: Birth & Age of the Universe

The two speakers, Dr. Andrei Linde and Dr. Robert Kirshner, were introduced by DR. DAVID SCHRAMM, Louis Block Professor in the Physical Sciences at the University of Chicago. Dr. Schramm noted, as with the geophysical sciences, cosmology is in a Golden Age. It has moved from being more of a branch of philosophy into being a true physical science. The technology involves not only large telescopes, but particle accelerators, deep underground experiments, satellites, and so on. Out of this multi-pronged approach to cosmology has come the establishment of a basic framework that the early universe was hot and dense, and there are three pillars to this framework: The Hubble Expansion (which will be talked about by Dr. Kirshner), The Microwave Background, and the "giant hydrogen bomb" model. Dr. Andrei Linde's talk will look at initial conditions which started the universe forming.

DR. ANDREI LINDE was one of the former Soviet Union's foremost cosmologists, and spent two years at CERN before moving to the United States to teach at Stanford University in 1992 where he now a Professor of Physics. Dr. Linde is one of the authors of inflationary theory, a more general theory than the standard theory of the Big Bang which, he feels, is wrought with too many problems, discussed in his talk. Inflationary theory is developing rapidly, and an overall shift is occurring in cosmology away from the Big Bang singularity. It has been believed that space-time was four-dimensional from the start and that it remains 4-D everywhere, it was believed that if the universe is closed its total size is on the order of its observable part, 10^{28} cm, and that in about 10^{11} years the whole universe will collapse and disappear in a Big Crunch. If, on the other hand, the universe is flat or open, then it is infinite, and it was commonly believed that its properties everywhere are approximately the same. Such a universe would exist without end, but after the decay of its protons, predicted by the unified elementary-particle theories, there would be no baryonic matter to support life of our type. The only possible choice seemed to be between the "hot ending" in the Big Crunch and the "cold ending" in infinite empty space. It seems more likely that the universe is an eternally existing, self producing entity, that it is divided into many mini-universes much larger than our observable portion, and the laws of low-energy physics and even the dimensionality of space-time may be different in each of

these mini-universes. "We cannot see the whole play in all its greatness, but we can try to imagine its most essential parts, and perhaps ultimately understand its meaning."

A question was raised about the idea Dr. Linde discussed that the universes are like bubbles -- can we see these other bubbles? In his characteristic way Dr. Linde told an old story: "someone asked God what for him is 10,000 years and God said 'oh, just one second' and then asked God 'what for you is \$10,000?' and God said 'just one cent' and then asked God 'please give me one cent' and God replied 'wait one second.'"

DR. ROBERT KIRSHNER is Professor of Astronomy at Harvard University and Chairman of Harvard's Astronomy Department. Dr. Kirshner addressed the topic "Age of the Universe." Dr. Kirshner is addressing one of the three pillars Dr. Schramm mentioned in his introduction, The Hubble Constant. The expansion rate of the universe is influenced by its density (the gravitational pull); the expansion rate has been estimated by cosmologists, but the gravitational pull is unknown. If it is above the "critical value" the ending will be a Big Crunch, and if it's below the critical value, the ending will be a Big Chill. There is a relationship between the age, the future, and the expansion rate. There are a variety of ways to get the age of the universe, from old stars, from planets, etc. Dr. Kirshner talked about making a measurement and how it's connected to the age of the universe. The Hubble Constant: velocities for galaxies are measured in kilometers per second, and distances are measured in megaparsecs. There is a density parameter, represented by Ω . If Ω is low the universe will expand forever, if Ω is high it will collapse at some future time, and the just-right case is where Ω is equal to 1. The geometry of the universe is also connected to this. Euclidean geometry is pretty good, but not perfect because of any curvature that may exist in the universe. Apparent brightness of objects in the solar system is measured, the flux (brightness) drops off as the square of the distance, and other information is needed. Very simply, things that can be picked out with the same brightness are called standard candles -- the Cepheids are pretty good for use as standard candles -- and this is the start to measuring distance from earth to solar objects. Through their work at Harvard, Dr. Kirshner and others are finding supernovae are better standard candles than are Cepheids. Hubbel was looking at globular clusters and thought they were stars, and so his number for measuring the age of the universe was off.

This concludes the summaries of the talks.

RADIO PILOT PROGRAM

A 30 minute pilot production, called "Science at the Summit" has been made possible with a \$150,000 grant given by the Sloan Foundation, \$50,000 of which was used toward the 1994 pilot. The remaining \$100,000 will be applied to the costs of successive radio programs also developed from the Scientist to Scientist Colloquium by Bogosian Productions in 1995 and 1996.

WGBH public radio station in Boston is interested in a series and is discussing potential services-in-kind as well as direct funding to ensure it. The narrator, Mr. Ira Flatow, who hosts the "Science Friday" program on WGBH may host live from the 1995 Colloquium. The 1994 pilot aired in at least a dozen cities, including Portland, San Francisco, Anchorage, Santa Monica, Boston, Ithaca, and Philadelphia.

EVALUATION SUMMARY

The 1994 meeting itself was a success, by all accounts. 40% of the 82 participants in the 1994 meeting returned their evaluation questionnaires with thoughtful and provocative comments. To summarize these responses:

- 68% found the integrated sessions on the brain the most professionally rewarding and stimulating. Many commented that these talks were some of the best they had ever participated in, and one scientist (Anthony Leggett, physicist, U. Illinois Urbana-Champaign), said he is considering looking into physics related problems in the area of hearing after listening to Dr. A. J. Hudspeth's talk.
- 65% of the respondents thought the interactions would have a direct impact on their future research endeavors, at least regarding future contacts and future communications; in the latter area especially to include scientists in other fields when they are representing their work outside their own academic departments.
- 95% thought Dr. Hudspeth gave the most effective talk. A transcript of that talk is enclosed with this letter. Dr. Hudspeth has given us permission to publish the talk for marketing purposes.
- A number of people suggested that the principle reason for funding the Colloquium is, to quote Paul Steinhardt at the University of Pennsylvania, "it is an effective forum for keeping leading scientists abreast of the most important scientific breakthroughs by a means which is much more effective than literature or conferences." A very timely comment comes from George Bell at Los Alamos: "Increasingly ... bureaucrats and/or scientists will be forced to choose between various disciplines for prioritization of funding. The better they are informed about the exciting thrusts in other fields, the wiser their decisions." Comments like these are common among participants.
- Suggested improvements to the format were to provide very specific instruction to the session moderators who need to play a stronger role in keeping interruptions to a minimum. It was also suggested that the Steering Committee work harder toward more diversity as far as people of color, as well as scientists from a greater variety of disciplines. These are particular areas of Committee and staff focus for the 1995 meeting.

THE FUTURE OF SCIENTIST TO SCIENTIST COLLOQUIUM

Dr. Paul Berg, Nobelist, Director of the Arnold and Mabel Beckman Center for Molecular and Genetic Medicine at Stanford University, is the chairman of the 1995 Colloquium Steering Committee. Under his direction the program is completed and all speakers and session moderators are confirmed (please see attached). Already, 50 scientists are planning to attend, most of them newcomers to the Colloquium.

The Keystone Center is proud of the success and popularity of the Scientist to Scientist Colloquium and feel it is an important event to continue, in spite of the effort it takes to raise the necessary funding. We are fortunate to have had the support of the Office of Naval Research, the National Institute of Environmental Health Sciences, the U.S. Department of Agriculture, the National Science Foundation, the Golden Family Foundation, the Alfred P. Sloan Foundation, the Smart Family Foundation, as well as the support of a few generous individuals.

It is our hope, that based on our accomplishments, that the Office of Naval Research will once again provide a grant to The Keystone Center in support of the Scientist to Scientist Colloquium.

THE KEYSTONE CENTER
1994 SCIENTIST TO SCIENTIST COLLOQUIUM
KEYSTONE, COLORADO, AUGUST 14 - 19

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** Serving on the 1994 Steering Committee*

THE KEYSTONE CENTER
SCIENTIST TO SCIENTIST COLLOQUIUM
1995 Program

<u>TOPICS</u>	<u>SPEAKERS</u>	<u>AFFILIATIONS</u>
BRAIN I. <i>Brain Function</i>	Francis Crick, Chair Antonio Damasio Terry Sejnowski Ursula Bellugi	Salk Institute University of Iowa Salk Institute Salk Institute
BRAIN II. <i>Memory</i>	Larry Squire, Chair Charles Stevens Matthew Wilson	UC San Diego Salk Institute MIT
PARTICLE PHYSICS	Jerome Friedman, Chair Howard Georgi William Carithers	MIT Harvard University Lawrence Berkeley Lab
CHEMISTRY	Jack Szostak, Chair Jacqueline Barton Gerald Joyce	MIT CalTech Scripps Research Institute
HUMAN ORIGINS	Owen Lovejoy, Chair Timothy White Stephen Jay Gould	Kent State UC Berkeley Harvard University
BIOLOGICAL MOTORS	Lucille Shapiro, Chair James Spudich Howard Berg	Stanford University Stanford University Harvard University
DARK MATTER	David Schramm, Chair Charles Alcock Michael Turner	University of Chicago Lawrence Livermore University of Chicago

DINNER SPEAKERS:

Doug Hofstadter on Games that Illustrate Philosophical Constructs of Science
Tom Stoppard on Science and Literature (tentative)